REMARKS

Claims 1, 3-9, 11-17, 22, 44, and 58-63 are pending and under examination. New claims 64 and 65 have been added. Support for new claims 64 and 65 can be found, for example, in Example 15 on page 75, Example 16 on page 79, Example 18 on page 84, and Example 22 on page 90. Accordingly, these new claims do not raise an issue of new matter and entry thereof is respectfully requested.

Applicants appreciate the indication by Examiner Angell that claims 1, 3-9, 11-17, 22, 44 and 58-60 are allowable.

The rejection of claims 61-63 under 35 U.S.C. § 112, first paragraph, as allegedly being directed to new matter and as allegedly lacking enablement is respectfully traversed. Applicants respectfully maintain that the support provided in the previous response is sufficient to support claims 61-63. First, the Office Action acknowledges that the specification supports a gapmer sequence that has "all of the above indicated limitations." Those indicated limitations (highlighted in bold on page 4 of the Office Action) appear to include ten 2'deoxynucleotides, five nucleotide "wings," 2'methoxyethyl (2'-MOE) nucleotides, phosphorothioate throughout the oligonucleotide, and all cytidine residues being 5-methylcytidines.

In the Office Action on page 4, it is asserted that the claims are broader in scope than what is disclosed because the claims do not recite all of the above elements. Applicants respectfully disagree for the reasons of record and as discussed below. In addition, Applicants respectfully disagree with the statement on page 4 of the Office Action that the claims are not limited to the wings being composed of 2'-MOE nucleotides, "the claims merely require that each wing comprise a 2'-MOE sugar." Applicants note for the record the recitation in claim 62 "wherein each nucleoside of each wing segment comprises a 2'-O-methyoxyethyl sugar" and respectfully submit that the interpretation that the claims "merely require that each wing comprise a 2'-MOE sugar" is incorrect.

In the previous response, support for the claims was indicated to be found in the Modifications section starting on page 29 of the specification, in Example 15 on page 75, as well as in Table 1 on page 76. In addition to the support previously provided of record, Applicants point to additional support in the present response in the interest of furthering prosecution. In

particular, additional support for claims 61-63 can be found, for example, in Example 16 on page 79, in Example 18 on page 84, and in Example 22 on page 90. These teachings in the specification clearly provide support for an antisense oligonucleotide comprising a gap segment consisting of ten linked deoxynucleosides, a 5' wing segment consisting of five linked nucleosides and a 3' wing segment consisting of five linked nucleosides, where the gap segment is positioned between the 5' wing segment and the 3' wing segment, wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; and wherein each internucleoside linkage is a phosphorothioate linkage, as recited in claim 62, as well as an antisense oligonucleotide where each cytosine is a 5-methylcytosine, as recited in claim 63.

Further support for claims 61-63 can also be found, for example, in Example 4, starting on page 55. The specification teaches at this passage:

> Chimeric oligonucleotides, oligonucleosides or mixed oligonucleotides/oligonucleosides of the invention can be of several different types. These include a first type wherein the "gap" segment of linked nucleosides is positioned between 5' and 3' "wing" segments of linked nucleosides and a second "open end" type wherein the "gap" segment is located at either the 3' or the 5' terminus of the oligomeric compound. Oligonucleotides of the first type are also known in the art as "gapmers" or gapped oligonucleotides.

The specification also teaches that "**[I]**t is not necessary for all positions in a given compound to be uniformly modified, and in fact more than one of the aforementioned modifications may be incorporated in a single compound or even at a single nucleoside within an oligonucleotide" (page 38, lines 24-29). The specification additionally teaches that "chimeric antisense compounds" contain two or more chemically distinct regions, each made up of at least one monomer unit (page 38, line 30, to page 39, line 3). The specification further teaches that "[C]himeric antisense compounds of the invention may be formed as composite structures of two or more oligonucleotides, modified oligonucleotides, oligonucleosides and/or oligonucleotide mimetics as described above. Such compounds have also been referred to in the art as hybrids or gapmers" (page 39, lines 22-27). The specification additionally teaches that an oligonucleotide refers to an oligomer or polymer of RNA, DNA or mimetics, chimeras, analogs and homologs thereof and can contain naturally occurring nucleobases, sugars and covalent internucleoside linkages as well as having non-naturally occurring portions which function similarly (page 15, lines 22-29). The specification also teaches modifications starting on page 29, including

modified internucleoside linkages (starting on page 29, line 32), modified sugars and internucleoside linkages (starting on page 32, line 1), and modified sugars (starting on page 33, line 1). Thus, the specification clearly provides sufficient teachings of a chimeric oligonucleotide having a gap segment consisting of linked deoxynucleosides, a 5' wing segment consisting of linked nucleosides, and a 3' wing segment consisting of linked nucleosides, where the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein each nucleoside of each wing segment comprises a modified sugar, as recited in claim 61.

Applicants respectfully maintain that the specification provides sufficient description and guidance to provide written description and enablement for claims 61-63. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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